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Date:	March 17, 2004
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Our Ref. No.:	PF-0738 USN
Your Ref. No.:	10/070,634
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Comments:

Docket No.: PF-0738 USN

Certificate of Transmission

I hereby certify that this paper is being facsimile transmitted to the attention of Examiner Charles L. Patterson, Jr., Group Art Unit 1652, U.S. Patent and Trademark Office to Facsimile No. 703-872-9306 on March 17, 2004.

By: _____ Printed: Lisa McDill

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Yue et al.

Title: HUMAN HYDROLYTIC ENZYMES

Serial No.: 10/070,634 Filing Date: March 1, 2002

Examiner: Patterson, C. Group Art Unit: 1652

Attn: Examiner Charles L. Patterson, Jr.
United States Patent and Trademark Office
Fax No.: 703-872-9306

TRANSMITTAL FEE SHEET

Sir:

Transmitted herewith are the following for the above-identified application:

1. Response to Restriction Requirement (19 pp.);
2. Information Disclosure Statement (2 pp.);
3. List of References cited, PTO-1449 (1 pg.); and
4. Two (2) References (1 - 2).

The fee has been calculated as shown below.

Claims	Claims After Amendment	-	Claims Previously Paid For	=	Present Extra	Other Than Small Entity Rate	Fee	Additional Fee(s)	
Total	20	-	20	=	0	x$18.00	0	$	0
Indept.	2	-	3	=	0	x$86.00	0	$	0
First Presentation of Multiple Dependent Claims:						+290.00	0	$	0
							Total Fee:	$	0

X No additional Fee is required.

___ Please charge Deposit Account No. **09-0108** in the amount of: $ 0

The Commissioner is hereby authorized to charge any additional fees required under 37 CFR 1.16 and 1.17, or credit overpayment to Deposit Account No. 09-0108. **A duplicate copy of this sheet is enclosed.**

Respectfully submitted,

INCYTE CORPORATION

Date: March 17, 2004

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Docket No.: PF-0738 USN

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Fax No.: 703-872-9306

RESPONSE TO RESTRICTION REQUIREMENT UNDER 35 U.S.C. 121

Sir:

This paper is responsive to the Restriction Requirement and Request for Election dated February 17, 2004, setting a 1-month term for response. Prior to examination of the application, please amend the above-identified application as follows.

Docket No.: PF-0738 USN

IN THE SPECIFICATION

Please add the following paragraph immediately after the title on page 1.

This application is a national stage application filed under 35 U.S.C. § 371 of International Application No. PCT/US00/24107, filed August 31, 2000 and published in English as WO 01/16334 on March 8, 2001, which claims the benefit of U.S. Provisional Application No. 60/151,819, filed September 1, 1999.

Docket No.: PF-0738 USN

IN THE CLAIMS

This listing of the claims replaces all prior versions of the claims in the application.

1. (Currently Amended) An isolated polypeptide ~~comprising an amino acid sequence~~ selected from the group consisting of:

a) a polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, and SEQ ID NO:14.

b) a polypeptide comprising a naturally occurring amino acid sequence ~~having~~ at least 90% ~~sequence identity~~ identical to an amino acid sequence selected from the group consisting of SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, and SEQ ID NO:14,

c) a biologically active fragment of a polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, and SEQ ID NO:14, and

d) an immunogenic fragment of a polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, and SEQ ID NO:14.

2. (Currently Amended) An isolated polypeptide of claim 1 comprising an amino acid sequence selected from the group consisting of SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, and SEQ ID NO:14.

3. (Original) An isolated polynucleotide encoding a polypeptide of claim 1.

4. (Original) An isolated polynucleotide encoding a polypeptide of claim 2.

5. (Currently Amended) An isolated polynucleotide of claim 4 comprising a polynucleotide sequence selected from the group consisting of SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, and SEQ ID NO:28.

6. (Original) A recombinant polynucleotide comprising a promoter sequence operably linked to a polynucleotide of claim 3.

7. (Original) A cell transformed with a recombinant polynucleotide of claim 6.

8. (Canceled)

9. (Original) A method for producing a polypeptide of claim 1, the method comprising:

a) culturing a cell under conditions suitable for expression of the polypeptide, wherein said cell is transformed with a recombinant polynucleotide, and said recombinant polynucleotide comprises a promoter sequence operably linked to a polynucleotide encoding the polypeptide of claim 1, and

b) recovering the polypeptide so expressed.

10. (Original) An isolated antibody which specifically binds to a polypeptide of claim 1.

11. (Currently Amended) An isolated polynucleotide ~~comprising a polynucleotide sequence~~ selected from the group consisting of:

a) a polynucleotide comprising a polynucleotide sequence selected from the group consisting of SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, and SEQ ID NO:28,

b) a polynucleotide comprising a naturally occurring polynucleotide sequence ~~having~~ at least 70% ~~sequence identity~~ identical to a polynucleotide sequence selected from the group consisting of SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID

NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, and SEQ ID NO:28,

c) a polynucleotide ~~sequence~~ complementary to a polynucleotide of a),

d) a polynucleotide ~~sequence~~ complementary to a polynucleotide of b), and

e) an RNA equivalent of a)-d).

12. (Canceled)

13. (Currently Amended) A method ~~for~~ of detecting a target polynucleotide in a sample, said target polynucleotide having a sequence of a polynucleotide of claim 11, the method comprising:

a) hybridizing the sample with a probe comprising at least 20 contiguous nucleotides comprising a sequence complementary to said target polynucleotide in the sample, and which probe specifically hybridizes to said target polynucleotide, under conditions whereby a hybridization complex is formed between said probe and said target polynucleotide or fragments thereof, and

b) detecting the presence or absence of said hybridization complex, and, optionally, if present, the amount thereof.

14. (Canceled)

15. (Currently Amended) A method ~~for~~ of detecting a target polynucleotide in a sample, said target polynucleotide having a sequence of a polynucleotide of claim 11, the method comprising:

a) amplifying said target polynucleotide or fragment thereof using polymerase chain reaction amplification, and

b) detecting the presence or absence of said amplified target polynucleotide or fragment thereof, and, optionally, if present, the amount thereof.

16. (Currently Amended) A composition comprising ~~an effective amount of~~ a polypeptide of claim 1 and a pharmaceutically acceptable excipient.

17. (Original) A composition of claim 16, wherein the polypeptide comprises an amino acid sequence selected from the group consisting of SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, and SEQ ID NO:14.

18. (Canceled)

19. (Currently Amended) A method ~~for~~ of screening a compound for effectiveness as an agonist of a polypeptide of claim 1, the method comprising:

a) ~~exposing~~ contacting a sample comprising a polypeptide of claim 1 ~~to~~ with a compound, and

b) detecting agonist activity in the sample.

20.-21. (Canceled)

22. (Currently Amended) A method ~~for~~ of screening a compound for effectiveness as an antagonist of a polypeptide of claim 1, the method comprising:

a) ~~exposing~~ contacting a sample comprising a polypeptide of claim 1 ~~to~~ with a compound, and

b) detecting antagonist activity in the sample.

23.-24. (Canceled)

25. (Original) A method of screening for a compound that specifically binds to the polypeptide of claim 1, said method comprising the steps of:

a) combining the polypeptide of claim 1 with at least one test compound under suitable conditions, and

b) detecting binding of the polypeptide of claim 1 to the test compound, thereby identifying a compound that specifically binds to the polypeptide of claim 1.

26. (Canceled)

27. (Canceled)

28. (Currently Amended) A method ~~for assessing~~ of screening for potential toxicity of a test compound, said method comprising:

a) treating a biological sample containing nucleic acids with the test compound;

b) hybridizing the nucleic acids of the treated biological sample with a probe comprising at least 20 contiguous nucleotides of a polynucleotide of claim 11 under conditions whereby a specific hybridization complex is formed between said probe and a target polynucleotide in the biological sample, said target polynucleotide comprising a polynucleotide sequence of a polynucleotide of claim 11 or fragment thereof;

c) quantifying the amount of hybridization complex; and

d) comparing the amount of hybridization complex in the treated biological sample with the amount of hybridization complex in an untreated biological sample, wherein a difference in the amount of hybridization complex in the treated biological sample is indicative of toxicity of the test compound.

29. (New) An isolated polynucleotide comprising at least 60 contiguous nucleotides of a polynucleotide of claim 11.

30. (New) A method of claim 13, wherein the probe comprises at least 60 contiguous nucleotides.

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REMARKS

I. Pending Claims

The Examiner listed the pending claims as "1-28" on the Office Action Summary. Applicants note that Claims 12, 14, 18, 20, 21, 24, 26, and 27 were canceled on the Transmittal filed March 1, 2002.

Claims 8 and 23 are canceled in this amendment. Claims 1, 2, 5, 11, 13, 15, 16, 19, 22, and 28 are amended. New Claims 29 and 30, whose subject matter corresponds to that of previously canceled Claims 12 and 14, are added in this amendment. Therefore, Claims 1-7, 9-11, 13, 15-17, 19, 22-23, 25, 28, and 29-30 are pending.

II. Restriction Requirement

In the Restriction Requirement, the Examiner requested Applicants to elect one of the following inventions:

Groups 1-13 (Claims 1-2, 16-17, 19-20, 22-23, and 25-26) drawn to a polypeptide of SEQ ID NO:2-14, a composition comprising the polypeptide, a method for screening a compound for effectiveness as an agonist or antagonist of the polypeptide, a composition comprising the agonist or antagonist, a method of screening a compound for binding or modulation of activity of the polypeptide, with the group number corresponding to the sequence number.

Groups 14-26 (Claims 3-7, 9, 11-15, and 27) drawn to a polynucleotide of SEQ ID NO:16-28, a host cell, a method for producing a polypeptide using the polynucleotide, a method for detecting the polynucleotide by using a probe or by amplifying the polynucleotide, a method for screening a compound for effectiveness in altering the expression of the polynucleotide, with the group number corresponding to the sequence number.

Groups 27-39 (Claim 8) drawn to a transgenic organism comprising SEQ ID NO:16-28, with the group number corresponding to the sequence number.

Groups 40-52 (Claim 10) drawn to an antibody that binds to SEQ ID NO:2-14, with the group number corresponding to the sequence number.

Groups 53-65 (Claims 18 and 21) drawn to a method for treating a disease associated with decreased expression of HYENZ, comprising administering SEQ ID NO:2-14, with the group number corresponding to the sequence number.

Groups 66-78 (Claim 24) drawn to a method for treating a disease associated with overexpression of HYENZ, comprising administering SEQ ID NO:2-14, with the group number corresponding to the sequence number.

Groups 76-91 (Claim 28) drawn to a method for assessing toxicity of a test compound comprising treating a sample containing nucleic acids with a test compound and hybridizing the nucleic acids with a probe of at least 20 nucleotides of SEQ ID NO:16-28, with the group number corresponding to the sequence number.

Applicants respectfully point out several errors in the complex Restriction Requirement. First, the numbering of the groups appears to be mistaken as groups are included which appear to refer to SEQ ID NO:10 and SEQ ID NO:24, although these sequences are not present in the claims as filed. Second, the groups include claims which were canceled on the Transmittal at the time of filing.

Applicants respectfully suggest that the following groups were intended and make their election using the following numbering scheme. If the Examiner intended otherwise, Applicants respectfully request the opportunity to address the Restriction Requirement in a second (non-Final) Restriction Requirement.

Groups 1-12 (Claims 1-2, 16-17, 19, 22-23, and 25), with respect to SEQ ID NO:2-9 and 11-14 respectively.

Groups 13-24 (Claims 3-7, 9, 11, 13, and 15), with respect to SEQ ID NO:16-23 and 25-28, respectively.

Groups 25-36 (Claim 8), with respect to SEQ ID NO:16-23 and 25-28, respectively.

Groups 37-48 (Claim 10) with respect to SEQ ID NO:2-9 and 11-14 respectively.

Groups 49-60 (Claim 28), with respect to SEQ ID NO:16-23 and 25-28, respectively.

Applicants believe that new Claims 29 and 30 would be included with new Groups 13-24.

Applicants hereby elect, with traverse, to prosecute new Groups 13-24 (Claims 3-7, 9, 11, 13, and 15) as well as new Claims 29 and 30, which are drawn to polynucleotides. Applicants reserve the right to prosecute the subject matter of non-elected claims in subsequent divisional applications.

Further, Applicants elect, with traverse, to prosecute claims related to the polynucleotide sequences encoding the polypeptide sequence of SEQ ID NO:12, which sequences include SEQ ID NO:26, and which sequences read on new Group 22 (Claims 3-7, 9, 11, 13, and 15), as well as new Claims 29 and 30. Applicants traverse both the restriction requirement and the obligation to elect a single sequence for prosecution for at least the following reasons.

A. The unity of invention standard *must* be applied in national stage applications

Section 1850 of the Manual of Patent Examining Procedure (original 8th edition, August, 2001, latest version February 2003) (hereinafter "M.P.E.P.") provides:

> ... [W]hen the Office considers international applications ... during the national stage as a Designated or Elected Office under 35 U.S.C. 371, PCT Rule 13.1 and 13.2 will be followed when considering unity of invention of claims of different categories without regard to the practice in national applications filed under 35 U.S.C. 111....
>
> In applying PCT Rule 13.2 to ... national stage applications under 35 U.S.C. 371, examiners should consider for unity of invention all the claims to different categories of invention in the application and permit retention in the same application for searching and/or preliminary examination, claims to the categories which meet the requirements of PCT Rule 13.2....

Id at page 1800-66.

M.P.E.P. section 1893.03(d) reiterates the Examiner's obligation to apply the Unity of Invention standard PCT Rule 13.2 instead of U.S. restriction/election of species practice:

> Examiners are reminded that unity of invention (not restriction) practice is applicable ... in national stage applications submitted under 35 U.S.C. 371.

Id at page 1800-156, column 2.

B. Specific provisions of the Administrative Regulations Under the PCT and the corresponding provisions of the M.P.E.P. strongly support a finding of unity of invention among all of the claims in the present case

1. Unity of Invention is accepted as between claims to polypeptide sequences and claims to the polynucleotide sequences which encode them

Example 17, Part 2 of Annex B to the Administrative Instructions Under the PCT provides that unity of invention is accepted as between claims to polypeptide sequences and claims to polynucleotide sequences encoding those polypeptides. Those Examples are cited in M.P.E.P. section 1893.03(d) at page 1800-156, column 2 ("[n]ote also examples 1-17 of Annex B Part 2 of the PCT Administrative Instructions...")

Thus, in the present case, unity of invention exists at least as between claims drawn to polypeptide sequences SEQ ID NO:2-9 and 11-14 (i.e., Claims 1-2, 16-17) and as to claims drawn to polynucleotide sequences which encode those polypeptides (i.e., Claims 3-7, 11, and 29).

Therefore, Applicants respectfully request that the Examiner withdraw the Restriction Requirement at least as to Claims 1-7, 11, 16, 17, and 29 and examine those claims in a single application.

2. Unity of invention exists with respect to dependent claims in the same claim category as the independent claim from which they depend

M.P.E.P. section 1850(A) which recites the provisions of paragraph (c) of Part 1 (entitled "Instructions Concerning Unity of Invention") of Annex B (entitled "Unity of Invention") to the Administrative Instructions Under the PCT, provides:

> **(A) Independent and Dependent Claims.**
> Unity of invention has to be considered in the first place only in relation to the independent claims in an international application and not the dependent claims. By "dependent" claim is meant a claim which contains all the features of another claim and is in the same category of claim as that other claim (the expression "category of claim" referring to the classification of claims according to the subject matter of the invention claimed for example, product, process, use or apparatus or means, etc.).
> If the independent claims avoid the prior art and satisfy the requirement of unity of invention, no problem of lack of unity arises in respect of any claims that depend on the independent claims. In particular, it does not matter if a dependent claim itself contains a further invention....

See M.P.E.P. section 1850(A) at page 1800-66. See also M.P.E.P. Appendix AI at page 63.

In the present case, Claims 2, 16, and 17, all of which depend from Claim 1, are all directed to compositions of matter, i.e., to products. All of these claims contain all of the

features of the independent claim. Further, as discussed above, there is unity of invention as between Claim 1 and Claim 11.

Thus, it is improper to restrict Claims 1, 2, 16, and 17 from Claims 3-7, 9, 11, 13, and 15, as the Examiner has done. Therefore, Applicants respectfully request that the Examiner withdraw the Restriction Requirement at least as to the composition of matter claims, and that at least those claims be considered together in a single application.

C. Unity of invention exists as between all of Applicants' claims

M.P.E.P. 1850 provides:

> Unity of invention exists only when there is a technical relationship among the claimed inventions involving one or more special technical features. The term "special technical features" is defined as meaning those technical features that define a contribution which each of the inventions considered as a whole, makes over the prior art. The determination is made based on the contents of the claims as interpreted in light of the description and drawings. Annex B also contains examples concerning unity of invention.
> Id at page 1800-66.

M.P.E.P. 1893.03(d) similarly provides:

> A group of inventions is considered linked to form a single general inventive concept where there is a technical relationship among the inventions that involves at least one common or corresponding special technical feature. The expression special technical features is defined as meaning those technical features that define the contribution which each claimed invention, considered as a whole, makes over the prior art. For example, a corresponding technical feature is exemplified by a key defined by certain claimed structural characteristics which correspond to the claimed features of a lock to be used with the claimed key. Note also examples 1-17 of Annex B Part 2 of the PCT Administrative Instructions as amended July 1, 1992 contained in Appendix AI of the MPEP.
>
> *Id* at page 1800-156.

In the present case, unity of invention exists among all of Applicants' claims. The claimed polypeptide sequences and the claimed polynucleotide sequences encoding them are corresponding technical features which are common to all of Applicants' claims, which serve to technically interrelate all of Applicants' claims, and which define the contribution over the prior art made by each of them. Thus, Applicants' claims are linked to form a single general inventive concept, and Applicants are therefore entitled to prosecute all of their pending claims in a single national stage application.

1. The claimed polypeptide sequences, and the claimed polynucleotide sequences encoding those polypeptide sequences, are corresponding technical features that are common to all of Applicants' claims and that serve to technically interrelate them

Applicants' claims recite *inter alia* the polypeptides SEQ ID NO:2-9 and 11-14, and polynucleotides encoding those polypeptides, which sequences include the polynucleotide sequences SEQ ID NO:16-23 and 25-28. See Table 1 of the specification. Applicants respectfully submit that the claimed polypeptide sequences SEQ ID NO:2-9 and 11-14, and the claimed polynucleotide sequences encoding them, are corresponding technical features, given that the former are encoded by the latter, and conversely, the latter encode the former.

Further, the claimed polypeptide and corresponding polynucleotide sequences are common to all of Applicants' claims, given that each claim refers to one or both either explicitly or implicitly, by virtue of depending from a claim which makes an explicit reference to the claimed sequences.

Moreover, the claimed polypeptide and corresponding polynucleotide sequences serve to technically interrelate all of Applicants' claims. Applicants' composition of matter claims (1-7, 10-11, 16-17, and 29) are drawn to either the sequences themselves (1 and 2, drawn to polypeptide sequences, and 3-5, 11, and 29, drawn to polynucleotide sequences), to compositions of matter which comprise the sequences as one element (6-7, drawn to recombinant polynucleotide sequences and transformed cells, respectively, and 16-17, drawn to pharmaceutical compositions), or to compositions of matter wherein the claimed sequences functionally limit the claimed subject matter (Claim 10, drawn to antibodies which specifically bind a polypeptide of Claim 1).

In Applicants' method claims (9, 13, 15, 19, 22, 25, 28, and 30), the claimed sequences serve as either the product of the claimed method (Claim 9, drawn to a method of polypeptide production) and/or as a reagent for performing the method (Claims 19, 22, and 25, drawn to methods of screening a compound for effectiveness as an agonist or antagonist of a polypeptide of Claim 1, or methods of screening for compounds which specifically bind a polypeptide of Claim 1; and Claims 13, 15, 28, and 30, drawn to methods of detecting a target polynucleotide in a sample and a method for assessing toxicity of a test compound).

Therefore, the claimed polypeptide and polynucleotide sequences are corresponding technical features which are common to all of Applicants' claims, and which serve to technically interrelate them.

In sum, the claimed polypeptide sequences and the claimed polynucleotide sequences which encode them are corresponding technical features which are common to all of Applicants claims, which serve to technically interrelate all of Applicants' claims, and which define the contribution over the prior art made by each of them. Thus, Applicants' claims are linked to form a single general inventive concept, and Applicants are therefore entitled to prosecute all of their pending claims in a single national stage application. Withdrawal of the restriction requirement in the present case is therefore respectfully requested.

2. The claimed polypeptide and polynucleotide sequences define the contribution made by each of Applicants' claims over the prior art

At page 3 of the Restriction Requirement, the Examiner has alleges that "[t]he polypeptides of Groups 1-13 [*sic*: new Groups 1-12] are not a special technical feature of the polynucleotides of Groups 14-26 [*sic*: new Groups 13-24] because the Acc No. 015416, cited in the PCT search report, discloses Groups 14-26." The Examiner reasons as follows: (1) the technical feature linking new Groups 1-24 is the claimed amino acid/nucleic acid sequences; (2) the sequences disclosed by the cited references (Acc No. 015416, cited in the PCT search report) ***allegedly*** teach polynucleotide fragments of SEQ ID NO:16); (3) the reference sequences anticipate the claimed amino acid/nucleic acid sequences; and therefore, (4) the claimed amino acid and nucleic acid sequences lack novelty.

Applicants respectfully disagree with the Examiner's reasoning. Applicants first wish to emphasize that it is those polypeptide sequences and/or those corresponding polynucleotide sequences in their ***entire*** form which provide the "common or corresponding special technical feature" linking all of the claims to form a single general inventive concept.

Applicants respectfully point out that the full-length polypeptide and corresponding full-length polynucleotide sequences recited in Claims 1 and 11, and the claims dependent thereon, are not anticipated by the sequences described by the cited references. First, none of the full-length polypeptide or polynucleotide sequences recited in Claim 1 and 11 are explicitly disclosed by the cited reference, which is the sequence of genomic DNA. Moreover, even assuming for purposes of argument that the reference sequences disclose polypeptide fragments which exhibit sequence identity with *fragments* of SEQ ID NO:2, neither SEQ ID NO:2 itself, nor any polynucleotide sequence which encodes SEQ ID NO:2, can be anticipated by those

fragments. Therefore, the contribution over the prior art represented by the full-length polypeptide and polynucleotide sequences is not negated by the cited references.

In sum, the claimed polypeptide sequences and the claimed polynucleotide sequences which encode them are corresponding technical features which are common to all of Applicants claims, which serve to technically interrelate all of Applicants' claims, and which define the contribution over the prior art made by each of them. Thus, Applicants' claims are linked to form a single general inventive concept, and Applicants are therefore entitled to prosecute all of their pending claims in a single national stage application. Withdrawal of the restriction requirement in the present case is therefore respectfully requested.

D. Method Claims

In the event that the Examiner does not apply the unity of invention standard to this national phase application, Applicants note that the invention encompassed by Claim 28 (new Groups 49-60) is drawn to methods of use of the polynucleotides of new Groups 13-24, and should be examined together with new Groups 13-24. These method claims recite a product (i.e., a polynucleotide), which is of the same scope as the claimed polynucleotides being searched by the Examiner. Therefore, it would not be an undue burden on the Examiner to examine this method claim since the searches for the claimed polynucleotides and this method claim would substantially overlap.

In addition, the method Claim 28 is entitled to rejoinder upon allowance of a product claim per the Commissioner's Notice in the Official Gazette of March 26, 1996, entitled "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai*, *In re Brouwer* and 35 U.S.C. § 103(b)" which sets forth the rules, upon allowance of a product claim, for rejoinder of process claims covering the same scope of products. See also M.P.E.P. 821.04 as follows.

> Where product and process claims drawn to independent and distinct inventions are presented in the same application, applicant may be called upon under 35 U.S.C. 121 to elect claims to either the product or process. . . The claims to the nonelected invention will be withdrawn from further consideration under 37 C.F.R. 1.142. . . . However, if applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims which depend from or otherwise include all the limitations of the allowable product claim will be rejoined.

E. The Election of Species Requirement

Applicants traverse the Election of Species Requirement for at least the following reasons.

The Examiner's attention is directed to the Patent Office's own requirements for Markush practice, set forth in the M.P.E.P. at § 803.02 regarding restriction requirements in Markush-type claims:

> **PRACTICE RE MARKUSH-TYPE CLAIMS**
>
> If the members of the Markush group are **sufficiently few in number or so closely related** that a search and examination of the entire claim can be made without serious burden, the examiner must examine all claims on the merits, even though they are directed to independent and distinct inventions. In such a case, the examiner will not follow the procedure described below and will not require restriction.
>
> Since the decisions in *In re Weber*, 580 F.2d 455, 198 USPQ 328 (CCPA 1978) and *In re Haas*, 580 F.2d 461, 198 USPQ 334 (CCPA 1978), **it is improper for the Office to refuse to examine that which applicants regard as their invention**, unless the subject matter in a claim lacks unity of invention. *In re Harnish*, 631 F.2d 716, 206 USPQ 300 (CCPA 1980); and *Ex parte Hozumi*, 3 USPQ2d 1059 (Bd. Pat. App. & Int. 1984). Broadly, **unity of invention exists where compounds included within a Markush group (1) share a common utility and (2) share a substantial structural feature disclosed as being essential to that utility**.
>
> This subsection deals with Markush-type generic claims which include a plurality of alternatively usable substances or members. In most cases, a recitation by enumeration is used because there is no appropriate or true generic language. A Markush-type claim can include independent and distinct inventions. This is true where two or more of the members are so unrelated and diverse that a prior art reference anticipating the claim with respect to one of the members would not render the claim obvious under 35 U.S.C. 103 with respect to the other member(s). In applications containing claims of that nature, **the examiner may require a provisional election of a single species** prior to examination on the merits. The provisional election will be given effect in the event that the Markush-type claim should be found not allowable. Following election, the Markush-type claim will be examined fully with respect to the elected species and further to the extent necessary to determine patentability. If the Markush-type claim is not allowable over the prior art, examination will be limited to the Markush-type claim and claims to the elected species, with claims drawn to species patentably distinct from the elected species held withdrawn from further consideration.
>
> As an example, in the case of an application with a Markush-type claim drawn to the compound C-R, wherein R is a radical selected from the group consisting of A, B, C, D, and E, the examiner may require a provisional election

> of a single species, CA, CB, CC, CD, or CE. The Markush-type claim would then be examined fully with respect to the elected species and any species considered to be clearly unpatentable over the elected species. If on examination the elected species is found to be anticipated or rendered obvious by prior art, the Markush-type claim and claims to the elected species shall be rejected, and claims to the nonelected species would be held withdrawn from further consideration. As in the prevailing practice, a second action on the rejected claims would be made final.
>
> On the other hand, should no prior art be found that anticipates or renders obvious the elected species, the search of the Markush-type claim will be extended. If prior art is then found that anticipates or renders obvious the Markush-type claim with respect to a nonelected species, the Markush-type claim shall be rejected and claims to the nonelected species held withdrawn from further consideration. The prior art search, however, will not be extended unnecessarily to cover all nonelected species. Should applicant, in response to this rejection of the Markush-type claim, overcome the rejection, as by amending the Markush-type claim to exclude the species anticipated or rendered obvious by the prior art, the amended Markush-type claim will be reexamined. The prior art search will be extended to the extent necessary to determine patentability of the Markush-type claim. In the event prior art is found during the reexamination that anticipates or renders obvious the amended Markush-type claim, the claim will be rejected and the action made final. Amendments submitted after the final rejection further restricting the scope of the claim may be denied entry. [emphasis added]

As can be seen from the above, it is clear that the present Restriction Requirement does not meet the Patent Office's own requirements.

First, it is improper for the Office to refuse to examine that which applicants regard as their invention, unless the subject matter in a claim lacks unity of invention. The polynucleotides encoding the polypeptides of SEQ ID NO:2-9 and SEQ ID NO:11-14 (including the polynucleotides of SEQ ID NO:16-23 and SEQ ID NO:25-28) are alternatives of a similar nature in that all of the claimed polynucleotide sequences encode human hydrolytic enzymes. As such, the claimed polynucleotides share the common property/activity of encoding polypeptides which carry out hydrolysis reactions. In addition, the polynucleotides of the instant invention share a common structure in that they are all polynucleotide molecules. Furthermore, the claimed polynucleotides share a common utility in, for example, toxicology studies based on expression profiling.

Second, even if the claims could be considered to be "Markush-type generic claims which include a plurality of alternatively usable substances or members," it is further noted that the M.P.E.P states that "A Markush-type claim can include independent and distinct inventions. This is true where two or more of the members are so unrelated and diverse that a prior art

reference anticipating the claim with respect to one of the members would not render the claim obvious under 35 U.S.C. 103 with respect to the other member(s). In applications containing claims of that nature, **the examiner may require a provisional election of a single species** prior to examination on the merits." This clearly applies in the present case.

Third the Examiner's attention is directed to the M.P.E.P. at § 803.04 (Restriction - Nucleotide Sequences, EXAMPLES OF NUCLEOTIDE SEQUENCE CLAIMS) which states:

> Applications claiming more than ten individual independent and distinct nucleotide sequences in alternative form, such as set forth in example (A), will be subject to a restriction requirement. Only the ten nucleotide sequences selected in response to the restriction requirement and any other claimed sequences which are patentably indistinct therefrom will be examined.

Applications claiming only a combination of nucleotide sequences, such as set forth in example (B), will generally not be subject to a restriction requirement. The presence of one novel and nonobvious sequence within the combination will render the entire combination allowable. The combination will be searched until one nucleotide sequence is found to be allowable. The order of searching will be chosen by the examiner to maximize the identification of an allowable sequence. If no individual nucleotide sequence is found to be allowable, the examiner will consider whether the combination of sequences taken as a whole renders the claim allowable.

Therefore, it is respectfully submitted that, upon searching and examining SEQ ID NO:26 and finding no prior art over which SEQ ID NO:26 can be rejected, the Examiner must extend the search of the Markush-type claim to include 9 additional non-elected species.

CONCLUSION

In light of the above remarks, Applicants submit that the present application is fully in condition for allowance. Early notice to that effect is earnestly solicited.

If the Examiner contemplates other action, or if a telephone conference would expedite allowance of the claims, Applicants invite the Examiner to contact the undersigned.

Applicants believe that no fee is due with this communication. However, if the USPTO determines that a fee is due or that an excess fee has been paid, the Patent Office is authorized to debit or credit (respectively) Deposit Account No. **09-0108**.

Respectfully submitted,
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